REMARKS

Claims 1-3, 12, 13, 34-35 and 41-43 are pending. Claims 14, 32, and 33 have been withdrawn. Claim 22 has been cancelled. Claims 1-3, 12, 16-21, 34-35 and 41-43 have been amended. Support for the amendments may be found in the claims as originally filed and in the specification at p. 38-39. Applicant notes that all amendments and cancellations of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the amended or cancelled Claims (or similar Claims) in the future.

1. Claims 1-3, 12, 13, 16-22, 34, 35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement;

2. Claims 1-3, 12, 13, 16-22, 34, 35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement;

3. Claims 2, 17-22, 34, 35, and 42 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite; and

4. Claims 3, 34, and 35 stand rejected under 35 U.S.C. §102 as allegedly being anticipated.

These rejections are addressed in order below.

1. The claims are enabled.

Claims 1-3, 12, 13, 16-22, 34, 35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The claims have been amended to specify that the cells are negative for CD34 and CD45, positive for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages. The method claims have also been amended to specify a passaging step wherein non-adherent cells are removed. Applicants respectfully submit that application of the *Wands* factors to the amended claims leads to the conclusion that the claims are enabled.

Nature of the Invention. The claims are directed to methods of obtaining stem cells from umbilical cord matrix, wherein the cells in the matrix material is cultured and cells from the

matrix material are selected by passaging. The selected cells express a distinct collection of markers and characteristics, in particular, the cells are negative for CD34 and CD45, positive for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages. The invention is generally directed to enriched populations or fractions of stem cells.

Breadth of the claims. The claims have been amended to specify that the cells express a distinct collection of markers. Applicants submit that these amendments render the Examiner's arguments moot. Furthermore, the claims do not require any level of homogeneity of the cells. In fact, with the exception of Claim 34, the claims are directed to cultures of cells comprising UCMS cells and to methods of obtaining fractions enriched with stem cells. Thus, the claimed compositions can comprise cells other than UCMS cells.

Guidance of the Claims; Working Examples. In general terms, the Examiner has correctly summarized the teachings of the specification at pages 4-5 of the office action, with several exceptions. The specification teaches isolation of umbilical cord matrix stem cells (UCMS cells) from multiple amniotic species. The specification further teaches in detail at pages 22-24 that the claimed UCMS cells are isolated as enriched fraction that grows out from the cultured UCM. The stem cells are selected following a low number of passages and cells that float 24 hours following typsinization, i.e., non-adherent cells, are removed (*see* Specification at pages 23-24, and claims as originally filed). Those cells can then be further fractionated, for example by clonal or other selection, to further isolate the UCMS cells. Specification at 23; Example 6. Importantly, the population of stem cells resulting from the selection are mostly, though not completely uniform, in contrast to the Examiner's arguments at page 6 of the Office Action. The specification clearly teaches how to obtain this population of cells, and one of ordinary skill in the art could perform the methods described in the specification and obtain the claimed cells. In particular, the specification teaches at p. 24 that the cells can be passaged following typsinization to provide UCMS cells.

State of the Art/Predicatability of the Art. The Examiner acknowledges that the specification teaches that the claimed cells express cKit, but then argues that the presence of cKit fails to provide sufficient teachings to define the claimed cells. This appears to be a written description type argument instead of an enablement argument. In particular, this argument does not appear to be applicable to method claims which merely claims a method of making a population of cells. A particular level of homogeneity of the cells produced by the method is not

required by the claims, nor is a particular level of homogeneity required to use the invention as the specification contains multiple example of use of cells made by the claimed methods. Nevertheless, in order to make the claims more clear, Applicants have amended the claims to specify that the cells produced by the method are negative for CD34 and CD45 (Specification at 39; Example 2). This serves to further define the cells claimed in the composition claims.

Applicants respectfully submit that the state of the art is such that the claimed populations of cells could be easily isolated using the methods taught in the specification and what was known in the art. The Examiner focuses on the alleged heterogeneity of the cells because some of the cells express Oct-4 and alkaline phosphatase. First, Applicants submit that the claimed cells do not express CD34 and CD45, are negative for CD34 and CD45, positive for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages, and are a homogenous population with respect to those characteristics. This is sufficient for enablement of the method and composition claims. Second, even assuming that the populations isolated by the claimed methods are heterogeneous, that does not undermine the enablement of the method claims or the ability of the person of ordinary skill in the art to practice the method claims to produce the a useful population of cells as taught in the specification.

The Examiner has treated enablement of the method claims and composition claims as being subject to the same analysis. However, there can be no doubt that a person of skill in the art can practice the method claims. Following the claimed steps to arrive at the claimed result is well within the skill in the art. The Examiner has not addressed this aspect of the claims. Moreover, the Applicants submit that the skilled artisan can make and use the claimed stem cells. As such, the composition claims are enabled. The composition claims (with the exception of claim 34) are to cultures that comprise UCMS cells. There is no homogeneity requirement in the claims. The Examiner has failed to recognize this important point. To be useful, the claimed cultures do not need to be homogenous. The claimed cultures need only to comprise cells with stem cells characteristics. That is what is claimed. A person of skill in the art would recognize that such cultures comprising UCMS cells could be made as described in the specification. Further, as taught in the specification (See Example 6), the cells can be further isolated to provide homogeneous populations.

The Amount of Experimentation Necessary. With respect to this factor, the Examiner argues that "there is no purification step taught that appears to result in one cell type. It appears

that the cells that are used in the working examples are heterogeneous populations of cells." Again, as just described, the claims do require that the population of cells be homogenous and homogeneity is not required for the cells to be useful. Analysis of the claims as if they require purification of the cells or homogeneity of cells is improper.

In any event, the claims have been amended to require the passaging of the cells and that the cells have specific markers. Furthermore, the specification teaches that the cells can be further purified by methods such as clonal selection (see Example 7). Thus, the Examiner's arguments with respect to the heterogeneous nature of the cells are misplaced.

Applicants submit that one of skill in the art can practice the claimed methods without undue experimentation. The Examiner has not alleged that there is a step in the method claims that would require undue experimentation on the part of one of skill in the art. Applicants submit that one of skill in the art could take umbilical cord matrix, culture the matrix as described, and derive the claimed population of cells. Undue experimentation is not required to practice the claimed methods. The Examiner has not established that a person of skill in the art cannot perform the method.

Likewise, the Examiner has not established that the specification does not teach methods for obtaining compositions comprising UCMS cells. The Examiner arguments focus on heterogeneity, but the claims do not require a defined homogeneity. The Examiner has not established that it would require undue experimentation to obtain the claimed compositions of cells. Indeed, the Examiner recognizes that the claimed population were obtained by the methods described in the application. With respect to claim 34, the specification does teach isolated human UCMS cells obtained by clonal selection (See Example 7).

Finally, Applicants have cancelled the claims to avian cells which makes that rejection moot.

For the foregoing reasons, Applicants submit that the enablement rejection should be withdrawn.

2. The claims have an adequate written description.

Claims 1-3, 12, 13, 16-22, 34, 35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The examiner argues that the "working examples in the specification do not differentiate between a

composition of Wharton's jelly cells, and isolated UCMS cells of the instantly claimed invention." As indicated in the interview on January 16th, 2007, the terms umbilical cord matrix and Wharton's jelly are used interchangeably in the specification. Claim 2 has been cancelled as the Examiner in the interview expressed concerns that claim 2 did not further limit claim 1. Claim 34 has also been amended to refer to "cells" isolated from Wharton's jelly. Furthermore, even with respect to isolated UCMS cells, the specification provides an adequate written description in the specification at page 23 for clonal isolation of UCMS cells and describes such clonal isolation in Example 6, page 49, which describes the isolated cells as having a "round, small, blast-like morphology."

The Examiner further argues that "it appears that the cells express markers that are expressed in hematopoietic cells, ES cells, as well as myofibroblast cells." As described in detail above, with the exception of Claim 34, the claims do not require homogenous populations of cells. The cells do express a variety of markers. This is why the presently claimed populations or fractions of cells are a unique, novel population of cells. The fact that the cells express a unique combination of markers does not undermine written description, and indeed, by providing such markers one of ordinary skill in the art can recognize that the inventors are in possession of the invention as claimed.

The Examiner also argues that "the breadth of the claims recites 'any stem cell' which encompasses pluripotent, multipotent and unipotent cells. Certain embodiments recite that the cells are capable of differentiation into derivatives of endoderm, ectoderm, or mesoderm (claim 34), but the disclosure fails to provide sufficient written description for this cell, in the context of the claimed invention." Applicants respectfully submit that the claims as amended, which recite the presence or absence of certain cell markers, are not directed to any stem cell, only those with the specified characteristics and markers. Thus, the Examiner's arguments are moot. Furthermore, Claim 34 is written so that the cells can differentiate into endoderm, ectoderm or mesoderm – there is no requirement that the cells differentiate into all three cell lineages.

The Examiner, consistent with established case law, indicates in the Office Action that "possession may be shown by actual reduction to practice, clear depiction of the claimed invention in a detailed drawing, or by describing the invention with sufficient, relevant, identifying characteristics (as it relates to the claimed invention as a whole) such that one of skill in the art would recognize that the inventor had possession of the claimed invention." Office

Action p. 9. This is precisely what Applicants have done. The specification describes the actual reduction to practice of the claimed methods and compositions, and in particular fractions of cells enriched with UCMS cells. The Examiner cannot dispute this fact, and indeed, admits at p. 5 of the Office Action that "the specification teaches methods of isolating UCMS cells by providing non-blood umbilical cord, adding cells from the tissue to a medium that contains factors that stimulate UCMS cells growth without differentiation." This is actual reduction to practice. Furthermore, the specification is goes onto to describe the morphology of the UCMS cell populations and a number of identifying characteristics such as the presence or absence of specific cell markers. Based on the working examples and description, one of skill in the art would recognize that the inventors had possession of the invention as claimed. Applicants request that this rejection be withdrawn.

3. The claims are definite.

Claims 2, 17-22, 34, 35, and 42 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Claims 2, 17, 24, 35 and 42 have been amended in response to this rejection. Accordingly, Applicants respectfully request withdrawal of this rejection.

4. The claims are not anticipated.

Claims 3, 34, and 35 stand rejected under 35 U.S.C. §102 as allegedly being anticipated by either Mitchell et al. or Thomson.

With respect to Mitchell et al., Applicants herein submit a Katz declaration to remove Mitchell et al. as a reference.

With respect to Thomson et al., the claims have been amended to specify that the claimed cells are UCMS cells, meaning cells isolated from the umbilical cord matrix. Thomson does not teach this limitation.

Accordingly, Applicants request that the anticipation rejection be withdrawn.

CONCLUSION

Applicants believe that the claims are in condition for allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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